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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|-----------------|-------------|----------------------|---------------------|
| 06/963,366      | 11/10/97    | HILLMAN              | A-64261-27D-1       |

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HM22/1110

EXAMINER

VANDER VEER, E

|          |              |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1644

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DATE MAILED:

11/10/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

|                              |                                  |                        |
|------------------------------|----------------------------------|------------------------|
| <b>Office Action Summary</b> | Application No.                  | Applicant(s)           |
|                              | 08/963,368                       | Nolan                  |
|                              | Examiner<br>F. Pierre VanderVegt | Group Art Unit<br>1644 |



Responsive to communication(s) filed on Aug 5, 1999

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claims

Claim(s) 16-28 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

Claim(s) \_\_\_\_\_ is/are allowed.

Claim(s) 16-26 and 28 is/are rejected.

Claim(s) 27 is/are objected to.

Claims \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All  Some\*  None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

### DETAILED ACTION

This application is a divisional of application S.N. 08/789,333, which is a divisional of application S.N. 08/589,108, which is a divisional of application S.N. 08/589,911.

Claims 16-28 are currently pending in this application.

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1. In view of the amendment filed August 5, 1999, only the following rejections are maintained.

#### *Claim Rejections - 35 U.S.C. § 103*

10 The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 16-22 and 28 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,639,595 to Mirabelli et al (A on form PTO-1449, of record) in view of Kaufman (U on form PTO-892).

20 The '595 patent teaches a library of plasmid vectors which contains random oligonucleotides contained a population of  $2.7 \times 10^8$  sequences (column 15, lines 11-24 in particular), which comprises at least  $10^8$  different nucleic acids. The '595 patent further teaches transfected mammalian cells with the library incorporated into the genome as evidenced by surface expression of proteins encoded by the library sequences (column 15, lines 40-55 in particular).

25 The '595 patent does not teach retroviral vectors. However, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to substitute retroviral vectors, which were well known at the time the invention was made, for the plasmid vectors of the '595 patent based upon the teachings of Kaufman. Kaufman teaches that methods of DNA transfer, which includes plasmids, usually transform 5-50% of the target cells and express the DNA transiently, ultimately losing the transferred DNA from the population (page 495 in particular). Kaufman teaches that retroviral vectors, on the other hand, have significant advantages, in that they can transduce genes into a variety of cell types and into a variety of species and can introduce nearly 100% of the host cells. One would have been motivated to substitute retroviral vectors for the plasmid vectors taught by the '595 patent based on the teaching of Kaufman that retroviral vectors allow the practitioner "to produce stable cell lines as a

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result of retrovirus integration into the host chromosome" (paragraph bridging pages 494 and 495 in particular).

Applicant's arguments filed August 5, 1999 have been fully considered but they are not persuasive.

5        Applicant argues this ground of rejection based upon the contention that the '595 patent teaches only antisense and phenotypic changes based upon the inserted antisense sequences. The Examiner respectfully disagrees with this position. As stated previously, the '595 patent further teaches transfected mammalian cells with the library incorporated into the genome as evidenced by surface expression of proteins encoded by the library sequences (column 15, lines 40-55 in particular). Applicant further contests the rejection based upon the teaching of Kaufman that protein expression from retroviral vectors is low in target cells. The Examiner maintains the position, however, because in the same paragraph, as stated previously, methods using retroviral vectors are superior to other known methods for transduction of host cells. It is respectfully submitted that the artisan would, in spite of low protein expression in host cells, still be motivated to use retroviral vectors based upon Kaufman's teaching that retroviral vectors are superior to other known methods for introducing DNA into cells for expression.

3.        Claims 16-26 and 28 stand rejected under 35 U.S.C. 103(a) as being unpatentable over  
20 U.S. Patent No. 5,639,595 to Mirabelli et al (A on form PTO-1449, of record) in view of  
Kaufman (U on form PTO-892) and Nilsson et al(V).

The '595 patent and Kaufman have been discussed supra. The combined references do not teach the expression of fusion proteins [claims 23-26]. Nilsson et al teaches that fusion proteins are constructed for a variety of purposes, such as increasing the stability of the product [claim 26], both during purification or in vivo use of the product (pages 570-571 in particular). Nilsson et al further teaches that fusion of a desired protein product with a 'handle' that has unique binding characteristics facilitates purification (rescue) of the desired protein so that the protein which confers a particular phenotype of interest on the host cell can be retrieved for further study [claim 25]. Nilsson et al also teaches that a further reason to construct a fusion protein would be for targeting of protein drugs (page 572 in particular)[claim 24]. It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of Nilsson et al with those of the '595 patent and Kaufman. One would have been motivated to combine these teachings with a reasonable expectation of success based

on the teachings of Nilsson et al that fusion proteins can be constructed for a variety of reasons ranging from protein recovery to therapeutic uses.

Applicant traverses this ground of rejection for the same reasons as those for the rejection supra, stating only that Nilsson et al does not correct the deficiencies in the combination of the '595 patent and Kaufman. For the reasons stated in paragraph 2, supra, the Examiner believes that said combination is not deficient. Accordingly, the ground of rejection stands.

***Allowable Subject Matter***

10 4. Claim 27 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

15 The prior art does not teach the introduction of a dimerization sequence into a fusion protein to express two copies of a peptide or two different peptides in the same host cell to effectively increase the size of the expressed peptide library.

***Conclusion***

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

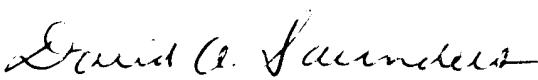
20 A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

30 6. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center

located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

5 Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and even-numbered Mondays (on 1999 365-day calender) from 7:00 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the  
10 Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

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F. Pierre VanderVegt, Ph.D.  
Patent Examiner  
Technology Center 1600  
November 8, 1999

  
DAVID SAUNDERS  
PRIMARY EXAMINER  
ART UNIT ~~182~~ 1644